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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/870,762	06/06/1997	BRADFORD J. DUFT	226/104	7328

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EXAMINER
DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
1645	28

DATE MAILED: 12/18/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/870,762	Duft et al.
Examiner	**Art Unit**
S. Devi, Ph.D.	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 10, 2001* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-6* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *24.*
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Applicants' Reply

1) Acknowledgment is made of Applicants' reply filed 05/18/01 (paper no. 26) in response to the non-final Office Action mailed 11/13/00 (paper no. 21).

Status of Claims

2) No claims have been amended.

Claims 1-6 are pending in the instant application and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Information Disclosure Statement

5) Acknowledgment is made of Applicants' supplemental Information Disclosure Statement filed 05/18/01 (paper no. 24). The information referred to therein has been considered and a signed copy is attached to this Office Action (paper no. 28).

Rejection(s) Maintained

6) The provisional rejection of instant claims (claims 1-6) made in paragraph 10 of the Office Action mailed 11/13/00 (paper no. 21) under the judicially created doctrine of double patenting over the claims (claims 1-15) of the pending application, SN 09/445,517, is maintained for reasons set forth therein. Applicants request that this provisional rejection be held in abeyance until the official notification of allowance in the instant or the co-pending application.

7) The rejection of claims 1-3 made in paragraph 11 of the Office Action mailed 11/13/00 (paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Rink *et al.* (US 5,739,106, already of record) ('106), is maintained for reasons set forth therein and herebelow.

Applicants' arguments have been carefully considered, but are not persuasive.

Applicants contend that the Office has not established a *prima facie* case of obviousness. Applicants state that Rink *et al.* ('106) do not teach any method of treating the disease of obesity, which involves food intake, i.e., caloric intake, as one of the factors. However, it should be noted that Rink's teaching is related to inhibiting food intake, suppressing appetite and controlling body weight, and therefore is directly relevant to what is described in the instant specification. It should also be noted that the instant application on page 13, first paragraph, states that treating or preventing obesity includes inhibition of weight gain and inducing weight loss in patients in need thereof. It is further stated that this is meant to include controlling weight for cosmetic purposes in humans, that is to control body weight to improve bodily appearance. Thus, the instant specification describes the claimed method as one of inducing weight loss and controlling body weight. The Rink's teaching of administration of amylin to induce appetite suppression, i.e., $\geq$ 50% inhibition in food intake as depicted in Figure 1 would result in improvement of bodily appearance and thus, meets the Applicants' description of controlling body weight. Therefore, Rink *et al.* is properly applied in the instant rejection under 35 U.S.C § 103.

Applicants further contend that Rink *et al.* ('106) do not teach or suggest the use of amylin agonist alone for controlling appetite in mice, or for treating obesity in humans. Applicants contend that Rink *et al.* ('106) instruct the need for amylin agonist-CCK agonist combinations, and therefore teach away from the use of amylin agonists. However, it should be noted that instant claims encompass the administration of either amylin or amylin agonist. Rink *et al.* ('106) was applied in a rejection under 35 U.S.C § 103(a), because Rink *et al.* disclosed a method of appetite suppression or inhibition of food intake by $\geq$ 50% by administering amylin alone. See particularly the blocked circles in Figure 1 corresponding to numbers 1 and 2 on the X-axis. Note that Figure 1 is entitled 'Dose Response for Appetite Suppression in Mice'. The Applicants' remarks with regard to Rink's use of amylin agonist alone for controlling food intake is misplaced, since the rejection of record concerned the use of amylin alone, as opposed to amylin agonist alone. In paragraph 11 of the Office Action mailed 11/13/00 (paper no. 21), Rink *et al.* ('106) was **not** cited as teaching a method of treating obesity by injecting amylin agonist alone, or a combination of amylin agonist and a CCK agonist, but by injecting amylin alone.

Instant claims require that the method of treating obesity involve administration of an anti-obesity agent, such as, amylin **or** amylin agonist. The claims are not limited to a method of treating obesity by administering amylin agonist alone, but the claims also encompass a method of treating obesity by the administration of amylin only. The Rink's ('106) teaching therefore meets the claim limitations under the 35 U.S.C. § 103 standard.

Applicants point out that contrary to the Office's position, the X axis in Figure 1 is on a log scale and that the coordinate "2" represents 100 microgram per kg. Applicants assert that the injection of amylin alone at 2.0 microgram/kg would have no effect on food intake. In response, Applicants are correct in that the X axis in Figure 1 is on a log scale. At item 11, the Office Action mailed 11/30/00 stated that "Figure 1 depicts that amylin alone when injected at 2 microgram/kg induced more than 50% inhibition in food intake at 30 minutes". This part of the Office Action did include a typographical error in that the word "log" was inadvertently left out while typing the phrase '2 microgram/kg'. Nevertheless, the sentence also mentioned about the induction of more than 50% inhibition in food intake by amylin alone at this dose. Figure 1 of Rink *et al.* ('106) entitled 'Dose Response for Appetite Suppression in Mice' is reproduced herebelow, with the parts relevant to the instant rejection highlighted using a yellow highlighter:

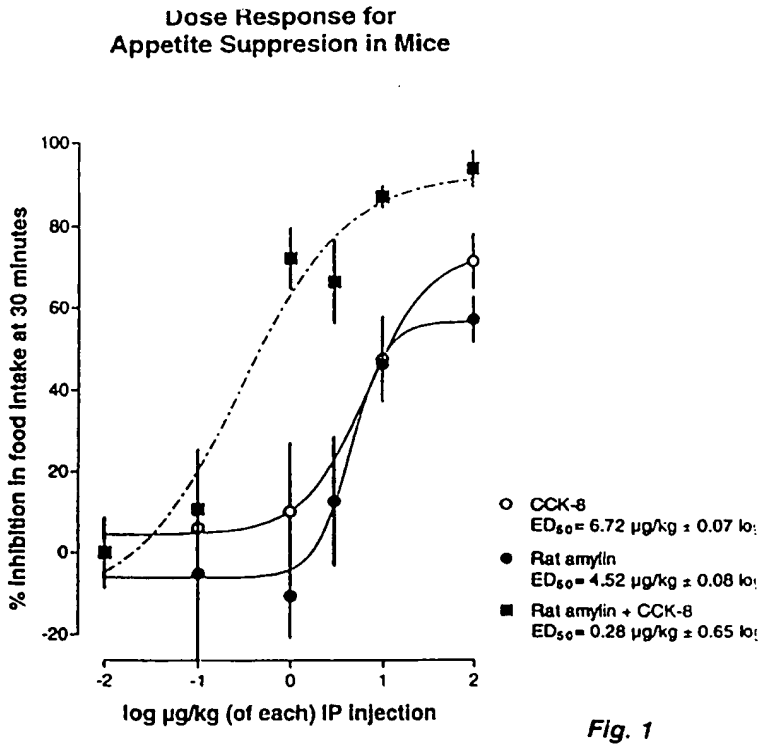

Fig. 1

From Figure 1, it is clear that at the dose referred to as "2" on the X-axis of Figure 1, amylin alone did indeed suppress food intake considerably. A similar response was observed by injection of amylin at a dose depicted as "1" on the X-axis of Figure 1. Irrespective of how many micrograms of amylin the coordinate "2" or "1" on the X-axis of Figure 1 represents, amylin alone (follow the blocked circle ● in Figure 1), at least at these two particular doses, did indeed inhibit food intake or suppress appetite. Even if the X coordinates 1 and 2 represented 10 and 100 microgram/kg respectively of amylin, it is clear that at these two doses, amylin alone induced $\geq$ 50% inhibition in food intake. It is important to note that the composition administered at these doses contained **only** amylin as indicated by the blocked circle (●). The amount of amylin injected is irrelevant, since the instant claims 1-3 do not require that amylin be administered in any specific amount or dose.

Applicants further contend that the words "alone and" in line 2 of the paragraph at column 22, lines 28-37 can only represent a typographical error. Applicants assert that the suppression in food intake is not significant. However, when one relates the statement to Figure 1 of Rink *et al.* ('106), as reproduced hereabove, one would realize that the Rink's ('106) reference to "-10.5±10.3% (not significant)" in lines 32 and 33 of column 22 is related to the appetite suppressing effect of amylin obtained at a dose designated as '0' on the X-axis of Figure 1, but not to doses depicted as "2" and "1" on the X-axis of Figure 1. This indicates to those skilled in the art that the dose depicted as '0' on the X-axis of Figure 1 was suboptimal or non-optimal in suppressing appetite or inhibiting food intake. It should be noted that in order to qualify as prior art under the 35 U.S.C. 103 standard, Rink *et al.* ('106) do not have to show that amylin alone suppresses appetite or inhibits food intake at every dose tested, since the instant claims do not require that a specific dose of amylin be administered in the claimed method.

Applicants further allege that the Office has not provided any reason why one of ordinary skill in the art at the time the invention was made would have modified Rink *et al.* to eliminate CCK from the methods of amylin agonist-CCK agonist administration. Applicants also allege that the Office is impermissibly using hindsight gained from Applicants' present teachings to bridge the gap from the methods of appetite suppression in mice by co-administration of an amylin agonist admixed with a CCK agonist to arrive at the presently claimed invention.

Applicants further contend that their invention is directed toward treatment of obesity in humans using amylin or an amylin agonist without requiring other components and that this is an indicia of unobviousness of the presently claimed invention. In response, there is no need for the Office to provide a reason for allegedly modifying Rink *et al.* to eliminate any element from Rink's composition, because the Office's rejection statement did not state that Rink's teachings were modified to eliminate CCK agonist. The term "CCK agonist" was never mentioned in the rejection made in paragraph 11 of the Office Action mailed 11/13/00. Instead, the rejection of record discussed the administration of amylin alone in the prior art method.

Applicants then allege that the general knowledge relied upon by the Office as providing motivation or suggestion would have been contrary to the teachings in the art at the time the invention was made. Applicants state that Amylin Pharmaceuticals had determined that it was amylin antagonists rather than amylin agonists that would find utility in the treatment of obesity. However, it is noted that, as explained above, Amylin Pharmaceuticals, i.e., Rink *et al.* ('106) had taught the administration of amylin alone to suppress appetite or inhibit food intake, i.e., to control body weight. Additionally, as already documented in the previous Office Actions, the state of the art at the time of the instant invention also indicated that amylin was used by many skilled in the art to reduce food intake, and as an appetite suppressant and as a peripheral satiety agent. A few examples of such references are cited again herebelow.

- Morley *et al.* (*Am. J. Physiol.* 267: R178-R184, July 1994, already of record) teach a method of reducing food intake in **obese** and diabetic subjects by administering upto 200 micrograms of amylin per kg (see abstract and page R179). Morley *et al.* (1994) also teach that amylin acts as a peripherally acting satiety agent (see abstract).

- Morley *et al.* (*Can. J. Physiol. Pharmacol.* 73: 1042-1046, 1995, already of record) teach that amylin decreases food intake in mice and rats when delivered both peripherally and directly into the CNS (see abstract).

- Rink *et al.* (WO 92/20367, already of record) expressly disclose that amylin can act as an appetite suppressant (see page 11, second full paragraph).

- Weisser *et al.* (*J. Clin. Pharmacol.* 37(6): 453-473, 19 June 1997, already of record) teach the association between amylin and obesity, and the potential role of amylin in

weight reduction (see page 467).

- Chance *et al.* (*Brain Res.* 539: 352-354, 1991, already of record) teach amylin as a suppressor of food intake (see entire document including abstract).

- Chance *et al.* (*Brain Res.* 607: 185-188, 1993, already of record) teach amylin as a suppressor of food intake (see entire document including abstract).

- Morley *et al.* (*Peptides* 12: 865-869, 1991, already of record) teach that administration of amylin decreases food intake in both diabetic and non-diabetic mice (abstract) and that amylin may have both central and peripheral sites of action. It is taught that amylin is considerably more potent than CGRP at suppressing food intake (see page 868).

Furthermore, the Applicants' own specification expressly acknowledges that the role of amylin as a food intake suppressor was known well before the effective filing date of the instant invention. For example, in the last paragraph on page 9, Applicants described the following:

> Injected into the brain, or administered peripherally, amylin has been reported to suppress food intake, e.g., Chance et al., *Brain Res.*, 539:352-354 (1991) and Chance et al., *Brain Res.*, 607:185-188 (1993), an action shared with CGRP and calcitonin. [Emphasis in original]

Thus, there were sufficient numbers of publications at the time of the instant invention that suggested the role of amylin as an appetite suppressant and as a peripheral satiety agent.

Applicants then contend that Rink (US 5,656,590) describes methods of treating anorexic patients by administering an amylin or an amylin analogue to increase weight. However, it should be noted that Applicants themselves acknowledge within the instant specification that several publications in the art have reported on the anorexia-causing ability of amylin. See the paragraph bridging pages 9 and 10 of the instant specification.

In sum, contrary to the Applicants' assertion, Rink *et al.* ('106) did demonstrate more than 50% inhibition of food intake by administration of amylin alone at a dose designated "2" on the X-axis of Figure 1 and almost 50% inhibition of food intake by administration of amylin alone at a dose designated "1" on the X-axis of Figure 1. Those skilled in the art would understand that about 50% inhibition in food intake would result in inhibition of weight gain, and improve bodily appearance. The rejection stands.

7) The rejection of claims 1-4 made in paragraph 12 of the Office Action mailed 11/13/00

(paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Arnelo *et al.* (Arnelo *et al.*, *Am. J. Physiol.* 271: 6 pt 2: R1654-R1659, December 1996) (Arnelo *et al.* I), or Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, January 1996) (Arnelo *et al.* II), is maintained for reasons set forth therein and herebelow.

8) The rejection of claims 5 and 6 made in paragraph 13 of the Office Action mailed 11/13/00 (paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Arnelo *et al.* (Arnelo *et al. Am. J. Physiol.* 271: 6 pt 2: R1654-R1659, December 1996) (Arnelo *et al.* I), or Arnelo *et al.* (*Scand. J. Gastroenterol.* 31: 83-89, January 1996) (Arnelo *et al.* II) as applied to claims 4 and 1, and further in view of Bennett *et al.* (US 5,955,443), is maintained for reasons set forth therein and herebelow.

Applicants' arguments have been carefully considered, but are non-persuasive.

Applicants contend that Arnelo's IAPP is a different molecule than amylin, and therefore one of skill in the art would not necessarily have applied Arnelo's teachings relating to IAPP to the amylin art. Applicants appear to allege that Arnelo *et al.* (II) mistakenly refer to IAPP as amylin. However, the art recognizes Arnelo's "IAPP" as a synonym for "amylin". For instance Wang *et al.* (*Diabetes* 42: 330-335, 1993) also refer to IAPP as "IAPP **or** amylin" (see abstract). Most importantly, Applicants themselves refer to Arnelo's (I and II) IAPP as 'amylin' in their specification. See for example, the paragraph bridging pages 9 and 10 of the instant specification.

Applicants state that Arnelo *et al.* (I) teach continuous or chronic administration of IAPP compared to the Applicants' invention. Applicants state that Figure 4 of Arnelo *et al.* (I) shows that rats consistently gained weight during the study, yet acknowledge that there was decreased body weight gain. Applicants assert that the effect of chronic IAPP administration in Arnelo *et al.* (I) was 'transient' over the reported eight day experiment and therefore would not suggest the presently claimed method. Applicants further opine that in Arnelo's (I) study the decrease of weight gain was due to a decrease in the average number of meals taken, but not due to a change in the mean meal size and the mean meal duration.

With regard to the teachings of Arnelo *et al.* (II), Applicants contend that Arnelo's (II) disclosure is unrelated to the Applicants' method, because it concerns administration of IAPP in

rats. Applicants refer to the doses of IAPP used by Arnelo *et al.* (II) and state that high doses of IAPP were ineffective. Yet Applicants acknowledge that chronic administrations of IAPP decreased body weight in the initial portion of the experiment. Applicants conclude that because the rats were increasing in body weight at the end of the study, one of ordinary skill in the art would not be motivated to apply Arnelo's (II) teachings to arrive at Applicants' claimed methods where sustained weight loss would be important.

In response, that the method described by Arnelo *et al.* (I and II) is directly applicable to the instantly claimed method is evident from the Applicants' own description provided in the paragraph bridging pages 9 and 10 of the instant application. In the paragraph bridging pages 9 and 10 of the instant specification, Applicants expressly state the following:

> Since the work described by the inventors herein with regard to the effect of amylin and amylin agonists to decrease body weight in humans, several publications have reported that infusion of amylin can cause anorexia in rats. See Arnelo et al., Am. J. Physiol. 40: R1654-R1659 (1996); Arnelo et al., Scan. J. Gastroenterol., 31: 83-89 (1966) [sic 1996]. [Emphasis in original].

It should be noted that the two references of Arnelo *et al.* (I) and (II) that are applied in the instant rejection are the same as the ones that are referred to by the Applicants in the paragraph bridging pages 9 and 10 of the instant specification, wherein Applicants mention of the infusion of 'amylin', as opposed to the allegedly distinct 'IAPP'.

Furthermore, it is important to note that instant claims are not limited to a method that involves non-chronic or discontinuous amylin administration. Instant claims are not limited to a method of obtaining sustained or non-transient weight loss in humans. Instant claims are not limited to a method of decreasing weight gain due to a change in the mean meal size, a change in the mean meal duration or a decrease in the average number of meals. The claims do not recite specific means or mechanisms by which the decrease in weight gain was accomplished. The claims do not exclude the administration of large doses of or non-continuous administration of amylin. The features upon which Applicants rely are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).* Therefore, Arnelo *et al.* (I) or Arnelo *et al.* (II) is properly applied in the instant rejection.

With regard to the teachings of Bennett *et al.* (US 5,955,433), Applicants submit that

Bennett's 'thrombin inhibition' patent does not supply any elements of the Applicants' invention that are missing from the Arnelo's (I and II) methods. Applicants contend that Bennett's teachings do not concern methods of treating obesity, the administration of an amylin or an amylin agonist and dosage frequencies or amounts related thereto.

In response, it should be noted that the reference of Bennett *et al.* was applied as a secondary reference in a rejection under 35 U.S.C § 103 and not as a single anticipatory reference under 35 U.S.C § 102. Bennett *et al.* was cited to document that the determination of effective doses of a pharmaceutical compound and the optimal frequency of its administration to a human subject based on the age, sex, weight, clinical condition and extent of a clinical condition in a human subject, are well known to those skilled in the art and are well within the realm of routine experimentation. Applicants appear to argue that the combination of references fails because the prior art does not have anticipatory references regarding all elements of the invention. The argument is not persuasive. At issue is whether the claimed method is obvious over the prior-art method, given the teachings of Arnelo *et al.* (I) or Arnelo *et al.* (II) and Bennett *et al.* As explained above, the invention as a whole, would have been obvious to a practitioner in view of the knowledge in the art at the time of the invention and the combined teachings of Arnelo *et al.* (I) or Arnelo *et al.* (II) and Bennett *et al.* It should be noted that what would reasonably have been known and used by one of ordinary skill in the art need not be explicitly taught. See *In re Nilssen*, 851 F.2d 1401, 7 USPQ2d 1500 (Fed. Cir. 1988). The test of obviousness is not express suggestion of the claimed invention in any and all of the references, but rather what the references taken collectively would reasonably have suggested to those of ordinary skill in the art presumed to be familiar with them. *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981).

9) The rejection of claims 1-6 made in paragraph 14 of the Office Action mailed 11/13/00 (paper no. 21) under 35 U.S.C § 103(a) as being unpatentable over Kolterman *et al.* (WO 96/40220) (Kolterman *et al.*, II) in view of Meglasson (US 5,134,164), is maintained for reasons set forth therein and herebelow.

Applicants' arguments have been carefully considered, but are non-persuasive.

Applicants contend that Kolterman *et al.* (II) teach methods of treating patients with type

II diabetes mellitus by administering an amylin agonist such as ^{25,28,29}pro-h-amylin, but do not advocate to one of ordinary skill in the art that the instant claimed methods of treating obesity can be accompanied by the administration of an amylin or an amylin agonist. Applicants submit that it is not clear how one of skill in the art would conclude that Kolterman's (II) dosage ranges and routes of administration would also be applicable to treatment of obesity. Applicants assert that one of skill in the art would not automatically apply the teachings of Kolterman *et al.* (II) to methods of treating obesity.

With regard to the teachings of Meglasson, Applicants contend that Meglasson lacks any suggestion that amylin or an amylin agonist can be used to treat obesity. Applicants state that Meglasson does not provide motivation necessary to arrive at the claimed invention.

In response, as clearly set forth in paragraph 14 of the Office Action mailed 11/13/00, the references of Kolterman *et al.* (II) and Meglasson were applied under 35 U.S.C § 103(a), as opposed to 35 U.S.C § 102. Kolterman *et al.* (II) taught a therapeutic method of administering subcutaneously 30 μg to 150 μg BID, of an amylin agonist, such as, ^{25,28,29}pro-h-amylin, s-calcitonin and h-amylin to hyperglycemic type II diabetic humans. Kolterman *et al.* (II) teach that AC137 (i.e., ^{25,28,29}pro-h-amylin) induces reduction in hyperglycemia in type II diabetic patients. It should be noted that Kolterman's (II) ^{25,28,29}pro-h-amylin is a subset of Applicants' generic amylin. Kolterman's (II) ^{25,28,29}pro-h-amylin is an amylin analogue. Meglasson was applied as a secondary reference under 35 U.S.C § 103(a) as explicitly disclosing that hyperglycemia also occurs in obesity as it does in non-insulin dependent diabetes mellitus, also known as NIDDM or type II diabetes, and that a compound that is useful in the treatment of hyperglycemia "could also be used to treat or prevent NIDDM" and "obesity" (see column 2, lines 21-25 and column 1, third paragraph). Given that amylin agonist, ^{25,28,29}pro-h-amylin, has already been identified in the art as a compound that is useful in the treatment of hyperglycemia and NIDDM (type II diabetes), or as a compound that reduces hyperglycemia in patients with type II diabetes or NIDDM, as taught by Koltermann *et al.* (II), it would have been obvious to one of ordinary skill in the art at the time the invention was made to use Kolterman's (II) method of reducing hyperglycemia for treating obesity to produce the instant invention, with a reasonable expectation of success, because Meglasson explicitly teaches that any compound that is useful in

the treatment of hyperglycemia could also be used to treat or prevent obesity. A skilled artisan would understand that Kolterman's anti-hyperglycemic compound, [25, 28,29]pro-h-amylin (i.e., an amylin agonist analogue) at the dose used, would also serve as an anti-obesity agent. Since there is an art-recognized general need for reducing the incidence of human obesity in general and/or diabetic population, one skilled in the art would have been motivated to use Kolterman's method of reducing hyperglycemia in humans to treat obesity for the expected benefit of reducing the increasing incidence obesity, because Meglasson explicitly teaches that any compound that is useful in the treatment of hyperglycemia could also be used to treat or prevent obesity. It should be noted that what would reasonably have been known and used by one of ordinary skill in the art need not be explicitly taught. See *In re Nilssen*, 851 F.2d 1401, 7 USPQ2d 1500 (Fed. Cir. 1988). The test of obviousness is not express suggestion of the claimed invention in any and all of the references, but rather what the references taken collectively would reasonably have suggested to those of ordinary skill in the art presumed to be familiar with them. *In re Keller*, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981).

Since the publication of Meglasson's patent, the prior art of Morley *et al.* (*Am. J. Physiol.* 267: R178-R184, July 1994); Morley *et al.* (*Can. J. Physiol. Pharmacol.* 73: 1042-1046, 1995); Rink *et al.* (WO 92/20367); Weisser *et al.* (*J. Clin. Pharmacol.* 37(6): 453-473, 19 June 1997); Chance *et al.* (*Brain Res.* 607: 185-188, 1993); Chance *et al.* (*Brain Res.* 607: 185-188, 1993) and Morley *et al.* (*Peptides* 12: 865-869, 1991), all taught the role of amylin in the suppression of appetite or suppression of food intake. As acknowledged by Applicants in the instant specification, "similar" to the body weight decreasing effect of amylin and amylin agonists shown by Applicants, several publications, i.e., Arnelo *et al.* (I) and Arnelo *et al.* (II) , had reported on the anorexia-causing role of amylin. Therefore, an amylin analogue, for example [25, 28, 29]pro-h-amylin, would also have been reasonably expected to produce the same effect.

Applicants resubmit the teachings of US patents 5,280,014 and 5,364,841 and allege that the Office has failed to take into account the teachings of these patents. However, a review of the prosecution record in the instant case indicates that the Office has fully addressed the teachings of these two patents. The US patents '014 and '841 were first made of record as relevant prior art by the Office via the first action on the merits mailed 09/16/98 (see page 8). The two patents

were then applied in the rejection of unamended claims 1 and 2 (see page 6 of the Office Action mailed 06/24/99), since the two patents taught a method of treating obesity in a subject by administering to a subject an effective amount of CGRP 8-37, which was known to serve as an *amylin agonist* in addition to having amylin antagonistic activities. Given this dual role, the '014 and '841 patents would not have diverged from and taught away from the invention at hand. Instead, these patents would only have lead those skilled in the art to use amylin agonists, at different doses or by different routes, to treat obesity, particularly since multiple published reports at the time had already taught an appetite suppressing or anorexia-causing role for amylin. It would have been obvious to those skilled in the art that substances serving as agonists to amylin would only fortify the appetite suppressing or anorexia-causing role for amylin. The disclosure from the applied art of Rink *et al.* ('106) (see above) is *prima facie* evidence for the body weight-controlling effects of amylin agonists, an example of which provided by Rink *et al.* ('106) was ^{25,28,29}pro-h-amylin. Additionally, when one takes Kolterman's (II) demonstration of the anti-hyperglycemic effects of ^{25,28,29}pro-h-amylin together with Meglasson's express suggestion that any compound which is useful in the treatment of hyperglycemia could also be used to treat or prevent obesity, it can hardly be argued that the instant claims are not *prima facie* obvious.

Remarks

10) Claims 1-6 stand rejected.

11) **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242.

13) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November 2001

S. DEVI, PH.D.
PRIMARY EXAMINER